Mefloquine (Lariam®)

Information for Clinicians

A Collaborative Effort of DHCC, AFIERA, NHEC, USACHPPM, & WRAMC

Mefloquine (Lariam®) is an anti-malarial drug effectively used to prevent malaria. It is FDA-approved for use in regions where local strains of malaria have developed a resistance to other anti-malarial agents such as chloroquine. Mefloquine is prescribed to over 350,000 Americans each year and a track record of relative safety and efficacy. Malaria, the disease mefloquine is used to prevent, is transmitted by mosquito, and remains a significant world health hazard, resulting in roughly two million deaths each year.

WHAT ARE THE INDICATIONS TO PRESCRIBE?

Mefloquine is taken once weekly to prevent or treat malaria in regions where the parasite is resistant to chloroquine. This information sheet addresses prophylactic mefloquine use. Alternatives to prophylactic mefloquine include doxycycline and Malarone® (atovaquone with proguanil), but these do not offer the same protection or advantages as mefloquine.

Patients who should not take mefloquine include those with a known hypersensitivity or allergy to mefloquine or related compounds (other quinoline methanol derivatives such as quinine, quinidine), a history of significant psychiatric illness, a cardiac conduction abnormality or dysrythmia, liver disease, or seizure disorder. Some occupational groups (e.g., aviators) may be restricted from taking prophylactic mefloquine. No anti-malarial provides 100% effective prevention. Therefore, critical prevention efforts include proper wear of the uniform and use of insect repellants on clothing and skin.

HOW IS IT USED TO PREVENT MALARIA?

For adults, the usual oral dosing regimen is 250 mg each week beginning one week before travel, continuing weekly during travel, and for 4 weeks after leaving an endemic area. Mefloquine should be taken with food and at least 8 oz. (240 mol) of water to enhance bioavailability and to minimize side effects, particularly stomach upset or vomiting. It should be taken for an additional four weeks after return from a malarial region. Steady state drug levels are reached after seven to eight weeks of consistent weekly dosing. Thus, side effects are more likely to occur within three to seven weeks of initiation. The elimination half-life is relatively long, lasting from 13 to 24 days.

WHAT SIGNIFICANT DRUG-DRUG INTERACTIONS SHOULD BE AVOIDED?

Providers should not prescribe mefloquine for patients taking medications that alter cardiac conduction (especially beta-blockers such as propranolol, atenolol, and metoprolol), anticonvulsant medications, drugs related to mefloquine (e.g. chloroquine, quinine, quinidine, and halofantrine), ampicillin, ampicillin/sulbactam, aurothioglucose, or the antipsychotic ziprasidone (Geodon®).

WHAT ARE THE COMMON SIDE-EFFECTS?

For most patients, mefloquine is well tolerated and offers the best protection in regions with chloroquine resistant malaria. Side effects occur in 3 to 25 per cent of patients, rates similar to chloroquine. Most side effects do not necessitate altering the type of prophylactic drug. Side effects can include insomnia, unusual dreams, lightheadedness, headache, vertigo, visual disturbances, ringing in the ear, rash, irritability, and gastrointestinal symptoms, such as nausea, vomiting, and diarrhea. If these effects occur, individuals should not engage in activities involving use of a weapon or operation of heavy equipment. If these effects persist or significantly impair functioning, consideration should be given to stopping the drug and changing to another anti-malarial.

WHAT ABOUT NEUROPSYCHIATRIC SIDE EFFECTS?

Rare instances of suicide in patients taking mefloquine have been reported but no studies have demonstrated a statistical association between mefloquine use and suicide, suicidal ideas, suicide attempts, or any other violent behavior. Patients with a history of psychiatric illness may be vulnerable to mefloquine-related psychiatric symptoms, and the package insert recommends against prescribing to patients with a history of psychiatric or alcohol problems.

Often, potential neuropsychiatric side effects are the greatest concern for patients. However, this type of side effect is quite rare. Side effects that can impair reaction time and thinking include convulsions, psychosis, nightmares, dizziness, confusion, anxiety, and depression. Studies indicate that these may occur in 1 in 2,000 to 1 in 13,000 people who receive prophylactic mefloquine. When neuropsychiatric side effects are suspected, the drug should be stopped. Once the drug is eliminated from the body, the effect usually goes away. Side effects may occur more commonly among those who consume alcohol while taking mefloquine, so patients should be carefully instructed to avoid alcoholic beverages.

Where can I get more information?

Mefloquine product safety information:
1) go to https://www.accessdata.fda.gov/scripts/medwatch/; 2) enter 'mefloquine' into the search engine window; and 3) click on the button labeled "GO!".

Mefloquine (Lariam®) package insert may be found on the web at:
http://www.rocheusa.com/products/lariam/pi.html

Malaria information may be found at the following web sites:
1. PDHealth.mil -- http://www.PDHealth.mil/Bosnia/endemic/malaria.asp
2. Centers for Disease Control & Prevention -- http://www.cdc.gov/ncidod/dpd/parasites/malaria/default.htm

Where can my patients get more information?
CHPPM Deployment Medication Information Sheet (DMIS) http://chppm-www.apgea.army.mil/dmis

DoD Deployment Health Clinical Center at Walter Reed Army Medical Center
Phone: 866.559.1627 Internet URL: http://www.pdhealth.mil/

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WHAT NEUROPSYCHIATRIC RED FLAGS SHOULD PRECIPITATE REFERRAL?

In the event a patient on mefloquine experiences suicidal ideation, depression, acute psychosis, or any of the other above-mentioned neuropsychiatric effects, the clinician should initiate an urgent medical referral including psychiatric assessment by a specialist. Under some deployed conditions, a psychiatric consultation may not be possible. In this situation, medical consultation with careful patient observation may be substituted. Mefloquine should be discontinued and replaced with another appropriate anti-malarial.

HOW CAN I REPORT ADVERSE DRUG EVENTS POTENTIALLY RELATED TO MEFLOQUINE?

Healthcare providers are encouraged to document and report known or suspected patient adverse drug events. The FDA has the primary responsibility for assuring the safety and efficacy of all regulated drug products. MedWatch, the FDA Safety Information and Adverse Event Reporting Program, serves both healthcare professionals and the public. MedWatch facilitates voluntary and confidential reporting of adverse events potentially related to various medications. Reporting can be done via the FDA website at **http://www.fda.gov/medwatch/report/hcp.htm**, telephone (1-800-FDA-1088), fax (1-800-FDA-0178) or mail. FDA MedWatch Form 3500 may also be completed online. It is also appropriate to notify the local Medical Treatment Facility Pharmacy and Therapeutics Committee of adverse events potentially due to prescribed or dispensed medications. This committee can review the event and forward the report to the FDA (see AR 40-3, Chapter 11, paragraph 11-6 d(9)).

WHAT TESTS SHOULD BE PERFORMED?

Baseline liver function tests are ideal though potentially impractical before deployment and should be repeated if clinical signs or symptoms suggest possible liver problems. An EKG should be performed for signs or symptoms suggestive of a potential cardiac problem. Animal studies have suggested changes in vision may occur with long-term mefloquine administration. Therefore, baseline vision testing is recommended and patients should be told to report vision problems to their provider. Repeat vision testing and eye examination should be should be performed if the patient reports vision changes or if administration is prolonged (twelve months or more).

CAN MEFLOQUINE BE USED DURING PREGNANCY OR BREASTFEEDING?

CDC has advised that mefloquine can be used in pregnancy and breastfeeding, but its use in the first trimester should be based on assessment of benefits versus risks. Pregnant women or those desiring to become pregnant while in malarial regions should be advised against travel to such locations. Women of childbearing age should use a reliable contraceptive during prophylaxis and for two months after the last dose to avoid conceiving. Consultation with a travel medicine or infectious disease expert is recommended for these patients.